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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/009,802	01/20/98	MCCARTHY	S MEI-008-1

HM22/0313
MILLENNIUM BIOTHERAPEUTICS, INC.
620 MEMORIAL DRIVE
CAMBRIDGE MA 02139

EXAMINER

YUCEL, I

ART UNIT	PAPER NUMBER
1636	12

DATE MAILED: 03/13/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.

09/009,802

Applicant(s)

McCarthy

Examiner

Remy Yucel

Group Art Unit

1636



☒ Responsive to communication(s) filed on Dec 20, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 61-88 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 61-88 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2, 3, 9

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Claims 61-88 are pending in the application.

This Office action is in response the communication filed 20 December 1999.

Election/Restriction

Applicant's election without traverse of Group III in Paper No. 10, filed 20 December 1999 is acknowledged.

Information Disclosure Statement

There have been five Information Disclosure Statements (IDS) filed in the instant application: 26 October 1998, paper 2; 17 October 1998, paper 3; 29 October 1998, paper 7; 17 December 1999, paper 8 and 20 December 1999, paper 9. Papers 7 and 8 are duplicates of papers 2 and 3, respectively will be placed in the file, but not considered further.

Paper 2 and paper 9 contain at least 145 references to GenBank accession numbers or to results of BLASTN searches with various sequences. These citations are not in conformance with MPEP 609 because, at the very least, they do not contain dates and/or authors. Secondly, given the extremely high number of citations for consideration (close to 150 such citations), Applicant should indicate the relevance of each of the references (for example, because the actual alignments from the BLASTN searches are not provided, the relevance of the citations is unknown to the Examiner). The Examiner will be happy to consider these references once the pertinent data have

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been provided. As Applicant will notice on the initialed PTO-1449, the Examiner has considered the balance of the references.

Specification

The specification contains several blanks, “_____”. The occurrences of these blanks are too numerous to count but are found at least at page 1, line 10, page 2 and pages 15-23 and 73. Applicant should review the entire specification and supply the missing information for **all** blanks.

The reference to the hyperlink found at page 28, line 10, “<http://www.ncbi.nlm.nih.gov>” must be removed is impermissible and requires deletion. This is effectively incorporates subject matter into the patent application by reference to a hyperlink (browser-executable code) which is considered to an improper incorporation by reference. Applicant is strongly urged to review the entire specification to remove any additional hyperlinks and/or other browser-executable codes which may be present in the specification.

At page 11, line 28 “differentaiton” should be --differentiation--. Applicant should review the specification for additional spelling errors.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is noted that the instant claims are drawn to CRSP-2 amino acid sequences.

Any response which does not fully address the above issues will be considered non-responsive.

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Claim Objections

The numbering of claims is not accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Because there were 61 originally filed claims, newly presented claims 61-87 have been renumbered as 62-88. Applicant must review the claims and include in his response, amendments correcting the dependencies of the pending claims. For example renumbered claim 63 depends from claim 61 when in fact, it should depend from claim 62. Also, the amendment should clarify the status of claim 61 (the last originally filed claim).

Claims 74 and 75 are duplicates of one another.

Any response which does not fully address the above issues will be considered non-responsive.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 61-88 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

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The instant claims are drawn to isolated polypeptides or polypeptide fragments of SEQ ID NO:5 which corresponds to the deduced amino acid sequence of CRSP-2, pharmaceutical compositions comprising CRSP-2 and assays identifying modulators of CRSP-2 activity. The specification teaches recombinant expression of a related polypeptide, CRSP-1, from its cDNA, but does not teach recombinant expression of CRSP-2. The instant disclosure does not provide specific functions for the CRSP-2 polypeptide, nor does it teach phenotypes which occur as a result in the over expression CRSP-2, nor does it teach phenotypes which occur as a result of under or no expression of CRSP-2, nor does the disclosure set forth any specific diseases or conditions which are related to the over or under expression of CRSP-2. The specification does not teach a single, specific and substantial utility for any CRSP protein/polypeptide, including the instantly claimed CRSP-2.

The specification sets forth various utilities for the claimed polypeptide (and nucleic acids which encode said polypeptide) including its use in forensic analyses. The utilities asserted by the specification; however, are not specific to the claimed invention and could be assigned to any nucleic acid or amino acid (polypeptide) obtained from nature.

Applicant's attention is also drawn to the teachings of Krupnik *et al.* (U, reference DQ on the IDS submitted 20 December 1999) which was published in a peer-reviewed journal over a year after Applicant's effective filing date of April 17, 1997, and lists the instant inventor as the corresponding author. Krupnik *et al.* teach that there are a family of proteins from human which are related to *Xenopus* Dickkopf-1 (xDkk-1) protein. Krupnik *et al.* hypothesize that in *Xenopus*,

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xDkk-1 protein *may* play a role in the induction of head structures in embryonic development. Krupnik *et al.* do not disclose the function or activity of xDkk-1. They further state that they have found a family of 4 human Dkk-related genes, hDkk-1 through hDkk-4. The instant CRSP-2 corresponds to hDkk-4. Krupnik disclose that these genes display a unique pattern of mRNA expression in human and mouse tissues and have highly conserved, (two) cysteine-rich domains. They also teach that hDkk-4 (CRSP-2) is secreted and undergoes proteolytic processing which results in the cleavage of the second cysteine-rich domain. Krupnik *et al.* also hypothesize that hDkk-1 and hDkk-4 *might* inhibit Wnt signaling. It is also noted that the instant specification is silent with respect to Wnt signaling and the role of CRSP proteins and that the specification does not mention Dkk proteins.

At page 312, Krupnik *et al.* cite another reference by Fedi *et al.* who have assayed for the activity of hDkk-1 in NIH3T3 cells and state “it will be of interest to characterize the activities of the mammalian DKK family in such assays, as well as to establish structure-function relationships and biochemical mechanisms of action.” The Krupnik *et al.* article cites recent advances in the biochemical analyses of Wnt proteins as potential facilitators of further characterization of Dkk proteins/polypeptides. This clearly indicates that even over a year after Applicant’s effective filing date of April 17, 1997, those of skill in the art still had not assigned specific functions to each of the human Dickkopf-related genes and their protein/polypeptide products.

In light of the above discussion, the asserted utilities disclosed in the instant specification do not fulfill the requirements of 35 U.S.C. 101.

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Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 61-88 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 62-69, 72, 73, 79-85, 87 and 88 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 62 and 63 are indefinite because it is not clear if the claims are drawn to polypeptide that is either at least 80 or 90% identical to the amino acid sequence of SEQ ID NO:5 or at least 80 or 90% identical to the amino acid sequence of SEQ ID NO:5 less the first nineteen amino acids or if the claims are drawn to a polypeptide that is either at least 80 or 90% identical

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to the amino acid sequence of SEQ ID NO:5 or is simply SEQ ID NO:5 less the first nineteen amino acids. Use of Markush language such as that found in claim 86 would clarify the claim, for example, “....identical to the amino acid sequence selected from the group consisting of”.

At page 7, the specification defines a “cysteine-rich region” as a protein domain with about 120-200 amino acid residues of which about 10-30 are cysteine residues. Because the specification defines “a cysteine-rich region” as a “cysteine-rich domain”, it is not clear what the distinction is between the two terms, thus it is not clear what the distinction is between that which is claimed in claims 64-69, 84 and 85 and dependent claim 88.

Claims 72 and 73 are problematic because it is not clear to what the recitation “or a complement thereof” refers. The claims are drawn to an isolated polypeptide, thus, by definition, the polypeptide does not have “a complement.” Further, the claimed polypeptide is encoded by a nucleic acid molecule comprising the sequence of SEQ ID NO:4 (claim 72) or SEQ ID NO:6 (claim 73)--by definition, the complement of SEQ ID NO:4 or SEQ ID NO:6 cannot encode the claimed polypeptide. Thirdly, the claims may also be interpreted as claiming the complement of either SEQ ID NO:4 or SEQ ID NO:6--which would be claiming a nucleic acid sequence, not a polypeptide, which is the elected invention.

Claims 79-83 contain the recitation “the fragment comprises” however, there is no antecedent basis for this recitation in claim 78 from which these claim depend.

In claim 87, the recitation “a polypeptide which is heterologous to the polypeptide of” renders the claim indefinite because it is not clear what is encompassed by the claim. The

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specification does not define what polypeptides are considered “endogenous” or “heterologous” to the recited polypeptides. It appears that Applicant wishes to claim a fusion polypeptide that comprises the CRSP-2 polypeptide or fragment thereof and any other polypeptide moiety. If this is the case, perhaps Applicant should consider using the language of originally filed claim 30 to obviate this rejection.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6 (d)). The Group 1600 FAX numbers are (703) 308-4242 or (703) 305-3014. Unofficial faxes may be sent to the examiner at (703) 305-7939. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Remy Yucel, Ph. D. whose telephone number is (703) 305-1998. The examiner can normally be reached on Monday through Fridays from 8:30 am to 5:00 pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott can be reached at (703) 308-4003.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.


Remy Yucel, Ph. D.
March 8, 2000